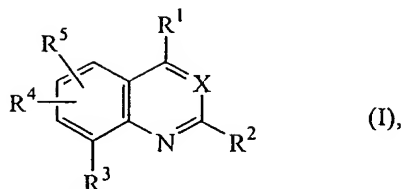


Claims

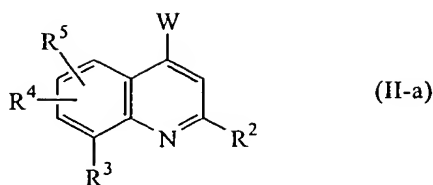
1. A compound of formula



- 5 including the stereoisomers and the pharmaceutically acceptable acid addition salt forms thereof, wherein
- X is N or CH;
- R¹ is C₁₋₆alkyl, NR⁶R⁷, OR⁷ or SR⁷;
- in case X is N then R² is hydrogen, C₁₋₆alkyl, C₁₋₆alkyloxy or C₁₋₆alkylthio;
- 10 in case X is CH then R² is C₁₋₆alkyl, C₁₋₆alkyloxy or C₁₋₆alkylthio;
- R³ is Ar¹ or Het¹;
- R⁴ and R⁵ are each independently selected from hydrogen, halo, C₁₋₆alkyl, C₁₋₆alkyloxy, trifluoromethyl, cyano, nitro, amino, and mono- or di(C₁₋₆alkyl)amino;
- 15 R⁶ is hydrogen, C₁₋₈alkyl, mono- or di(C₃₋₆cycloalkyl)methyl, C₃₋₆cycloalkyl, C₃₋₆alkenyl, hydroxyC₁₋₆alkyl, C₁₋₆alkylcarbonyloxyC₁₋₆alkyl or C₁₋₆alkyloxyC₁₋₆alkyl;
- R⁷ is C₁₋₈alkyl, mono- or di(C₃₋₆cycloalkyl)methyl, Ar²CH₂, C₁₋₆alkyloxy-C₁₋₆alkyl, hydroxyC₁₋₆alkyl, C₃₋₆alkenyl, thienylmethyl, furanylmethyl,
- 20 C₁₋₆alkylthioC₁₋₆alkyl, mono- or di(C₁₋₆alkyl)aminoC₁₋₆alkyl, di(C₁₋₆alkyl)amino, C₁₋₆alkylcarbonylC₁₋₆alkyl;
- or R⁶ and R⁷ taken together with the nitrogen atom to which they are attached may form a pyrrolidinyl, piperidinyl, homopiperidinyl or morpholinyl group, optionally substituted with C₁₋₆alkyl or C₁₋₆alkyloxyC₁₋₆alkyl; and
- 25 Ar¹ is phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, C₁₋₆alkyl, trifluoromethyl, hydroxy, cyano, C₁₋₆alkyloxy, benzyloxy, C₁₋₆alkylthio, nitro, amino and mono- or di(C₁₋₆alkyl)amino;
- Het¹ is pyridinyl; pyridinyl substituted with 1, 2 or 3 substituents each independently selected from halo, C₁₋₆alkyl, trifluoromethyl, hydroxy, cyano,
- 30 C₁₋₆alkyloxy, benzyloxy, C₁₋₆alkylthio, nitro, amino, and mono- or di(C₁₋₆alkyl)amino; and
- Ar² is phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, C₁₋₆alkyl, C₁₋₆alkyloxy, di(C₁₋₆alkyl)aminoC₁₋₆alkyl, trifluoromethyl;

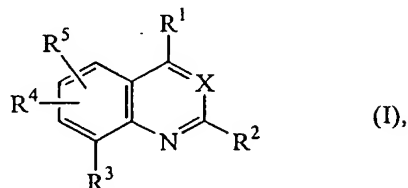
with the proviso that 2,4-dimethyl-8-(2-nitrophenyl)-quinoline is not included.

2. A compound according to claim 1 wherein R¹ is OR⁷ or SR⁷ and R⁷ is C₁₋₆alkyl; or R¹ is NR⁶R⁷ and R⁶ is hydrogen or C₁₋₆alkyl, and R⁷ is C₁₋₆alkyl or C₃₋₆cycloalkylmethyl; R² is C₁₋₆alkyl; R³ is a phenyl substituted with 1, 2 or 3 substituents each independently selected from C₁₋₆alkyl, C₁₋₆alkyloxy or halo, or R³ is a pyridinyl substituted with 1, 2 or 3 substituents each independently selected from C₁₋₆alkyl or di(C₁₋₆alkyl)amino; and R⁴ or R⁵ are each independently selected from hydrogen or C₁₋₆alkyl.
3. A compound according to any of claims 1 to 2 wherein R¹ is NR⁶R⁷ wherein R⁶ is C₂₋₄alkyl and R⁷ is C₂₋₄alkyl or cyclopropylmethyl; R² is C₁₋₂alkyl; R³ is phenyl substituted with 1, 2 or 3 substituents each independently selected from hydrogen, halo or C₁₋₆alkyl.
4. A compound according to any of claims 1 to 2 wherein R¹ is NR⁶R⁷ wherein R⁶ is C₃₋₄alkyl and R⁷ is C₃₋₄alkyl or cyclopropylmethyl; R² is methyl; R³ is 3-pyridinyl substituted on the 4- and/or 6-position with methyl or dimethylamino.
5. A compound according to claim 1 wherein the compound is 2-methyl-4-dipropylamino-8-(2',4'-dichlorophenyl)-quinoline; or 2-methyl-4-(*N*-propyl-*N*-cyclopropanemethyl)amino-8-(2',4'-dichlorophenyl)-quinoline; a stereoisomeric form or a pharmaceutically acceptable acid addition salt thereof.
6. A composition comprising a pharmaceutically acceptable carrier, and as active ingredient a therapeutically effective amount of a compound as claimed in any one of claims 1 to 5.
7. A process for preparing a composition as claimed in claim 6 wherein a therapeutically effective amount of a compound as claimed in any one of claims 1 to 5 is intimately mixed with a pharmaceutically acceptable carrier.
8. A compound according to any one of claims 1 to 5 for use as a medicine.
9. A compound of formula (II-a) wherein the radicals X, R², R³, R⁴ and R⁵ are as defined in claim 1 and W is halo, mesyloxy or tosyloxy; a stereoisomeric form or an acid addition salt form thereof.



10. The use of compounds of formula

5

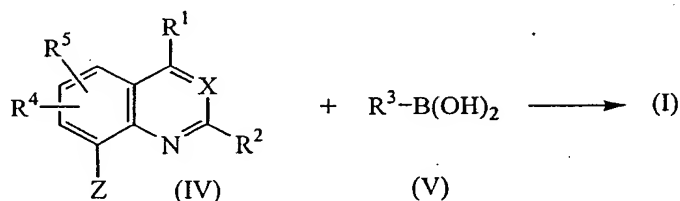


including the stereoisomers and the pharmaceutically acceptable acid addition salt forms thereof, wherein X, R¹, R², R³, R⁴ and R⁵ are as defined in claim 1, including the compound 2,4-dimethyl-8-(2-nitrophenyl)-quinoline, for the manufacture of a medicament for treating physiological conditions or disorders arising from the hypersecretion of corticotropin-releasing factor (CRF).

10

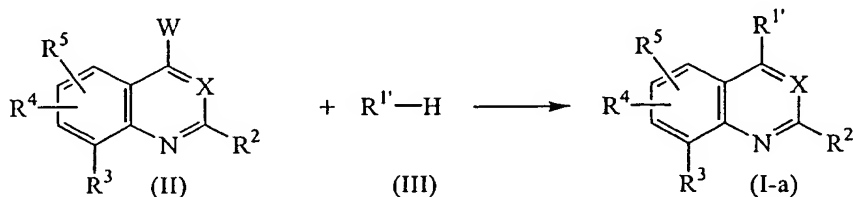
11. A process of preparing a compound of formula (I) as claimed in claim 1 wherein
a) intermediates of formula (IV) are reacted with intermediates of formula (V) under Suzuki coupling conditions;

15



20

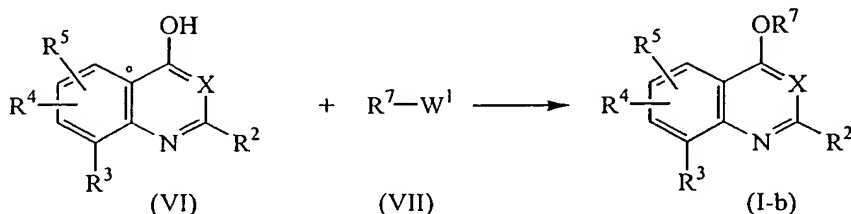
b) an intermediate of formula (II) is reacted with an intermediate of formula (III), wherein R^{1'} has the meaning of R¹ other than C₁₋₆alkyl, thereby yielding compounds of formula (I-a);



25

c) an intermediate of formula (VI) is *O*-alkylated with an intermediate of formula (VII) in a reaction-inert solvent and in the presence of a suitable base, yielding compounds of formula (I-b), defined as compounds of formula (I) wherein R¹ is OR⁷,

5



wherein in the above reaction schemes the radicals R¹, R², R³, R⁶, R⁷ and X are as defined in claim 1, Z is bromo or iodo and W and W¹ are appropriate leaving groups;

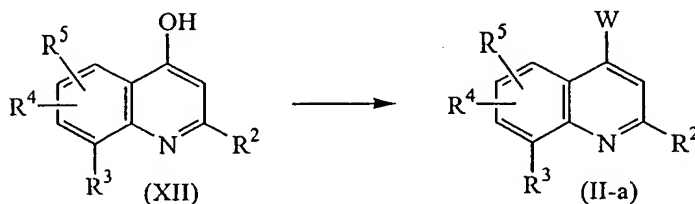
10

or, if desired, compounds of formula (I) are converted into each other following art-known transformation reactions; and further, if desired, compounds of formula (I) are converted into an acid addition salt by treatment with an acid, or conversely, the acid addition salt forms are converted into the free base by treatment with alkali; and, if desired, preparing stereochemically isomeric forms thereof.

15

12. A process of preparing a compound of formula (II-a) as claimed in claim 9 wherein a) an intermediate of formula (IX) is treated with methanesulfonyloxy chloride, benzenesulfonyloxy chloride or a halogenating reagent such as, e.g. SOCl₂ or POCl₃;

20



25

wherein in the above reaction scheme the radicals X, R², R³, R⁴ and R⁵ are as defined in claim 1 and W is halo, mesyloxy or tosyloxy;

or, if desired, compounds of formula (II-a) are converted into each other following art-known transformation reactions; and further, if desired, compounds of formula (II-a) are converted into an acid addition salt by treatment with an acid, or conversely, the acid addition salt forms are converted into the free base by

30

treatment with alkali; and, if desired, preparing stereochemically isomeric forms thereof.

- 5 13. A method of antagonizing a CRF receptor in a warm-blooded animal, comprising administering to the animal an effective amount of a compound of any of claims 1 or 5.
- 10 14. A method of treating a disorder manifesting hypersecretion of CRF in a warm-blooded animal, comprising administering to the animal an effective amount of a compound of any of claims 1 or 5.
- 15 15. The method of claim 14 wherein the disorder is selected from depression, an anxiety-related disorder, a feeding disorder, stress-induced immune suppression, stroke, Cushing's disease, infantile spasms, epilepsy, seizure, an inflammatory condition.
16. The method of claim 15 wherein the feeding disorder is anorexia nervosa, bulimia or irritable bowel syndrome.